

Asthma mortality in Australia 1920-94: age, period, and cohort effects

Richard Taylor, Elizabeth Comino, Adrian Bauman

Abstract

Study objective—To investigate asthma mortality during 1920-94 in Australia in order to assess the relative role of period and birth cohort effects.

Design—Asthma mortality (both sexes) was age standardised and examined for changes over time. The data were also examined for age, period, and cohort (APC) effects using Poisson regression modelling.

Setting—National Australian mortality data.

Participants—Population (both sexes) aged 15-34 years, 1920-94.

Main results—Age adjusted period rates indicate an increase in asthma mortality during the 1950s, and increases and subsequent falls (epidemics) during the mid 1960s and late 1980s. APC modelling suggested an increasing cohort effect (adjusted for both age and period) from the birth cohort 1950-54 onwards. Period effects (adjusted for age and cohort) are characterised by an increase in the 1950s (possibly due to changes in diagnostic labelling), minimal or no increases in the mid 1960s and late 1980s (where period peaks had been noted when data were adjusted for age only), and declines in mortality risk subsequent to the periods where age-period analysis had noted increases. Thus, in Australia, some of the mid 1960s epidemic in asthma deaths, and all of the late 1980s mortality increase, seem to be attributable to cohort effects.

Conclusions—The increase in asthma mortality cohort effect is consistent with empirical evidence of recent increases in prevalence (and presumably incidence) of asthma in Australia, and suggests the need for more research into the underlying environmental aetiology of this condition.

(*J Epidemiol Community Health* 1997;51:408-411)

Asthma is an important cause of morbidity in many developed countries. In recent years epidemiological evidence has accumulated that the prevalence has increased.^{1,2,3} In Australia, serial monitoring of asthma prevalence among adults using identical techniques has found increased diagnosis among adults aged 18-39 years.⁴ Among children an increased prevalence of asthma and airway abnormalities has been observed over a 10 year period.⁵

Analysis of asthma mortality is an important monitoring tool for assessing the outcome of the disease and its management by health ser-

vices at a population level. Period trends in age standardised asthma death rates in Australia have indicated three periods of increase. The first occurred in the 1950s and was probably attributable to diagnostic and coding changes, the second, in the mid 1960s, was followed by a decline,⁶ and the third was a lesser peak which occurred in the late 1980s.⁷ Although evidence is contradictory, clinical management practices favouring use of bronchodilator aerosols and/or particular medications may have been implicated in the latter two increases.^{8,9} Australia is one of the few developed countries where aerosol bronchodilators are available over the counter (without a doctor's prescription) from pharmacies. This situation has existed since 1976 in New South Wales, the largest state, and by 1985 in all other states. Isoprenaline (and the forte version) was available in Australia during the 1960s; its use declined markedly with the introduction of the β_2 agonists around 1970, and it has not been supported by subsidisation through the government's Pharmaceutical Benefits Scheme since then. Fenoterol use, which was implicated in changes in asthma mortality New Zealand⁹ during the 1980s, was very low in Australia.

Recent research suggests that the prevalence of asthma is increasing in the Australian population,^{10,11} which implies increase in incidence, since mortality is very low, even during peak periods.

We examine trends in asthma mortality (ages 5-34 years) for 1920-94, and explore the possible existence of underlying birth cohort effects which would not necessarily be obvious from plots of age adjusted data in relation to period. Cohort effects usually imply environment factors in aetiology, which occur early in life and subsequently produce effects. Period effects are operative at the time of death on all ages, and may be related to changes in medical management and also to diagnostic classification and coding.

Age, period, and cohort (APC) analysis techniques have been developed in recent years^{12,13} and have been used to study trends in cancer occurrence^{14,15,16} and asthma mortality in England.¹⁷ The techniques enable the influence of a single effect to be examined while controlling for the effect of the remaining two effects. When the effect of age and period was controlled, Burney¹⁷ showed an increase in mortality with each cohort born since the 1940s in England.

Methods

DATA

The asthma deaths and population for both sexes, aged 5-34 years, by five year age group

Department of
Public Health and
Community Medicine,
Faculty of Medicine,
Edward Ford Building
A27, University of
Sydney, NSW 2006,
Australia.
R Taylor

School of Community
Medicine, Faculty of
Medicine, University
of New South Wales,
Australia
E Comino
A Bauman

Correspondence to:
Associate Professor
R Taylor.

Accepted for publication
December 1996

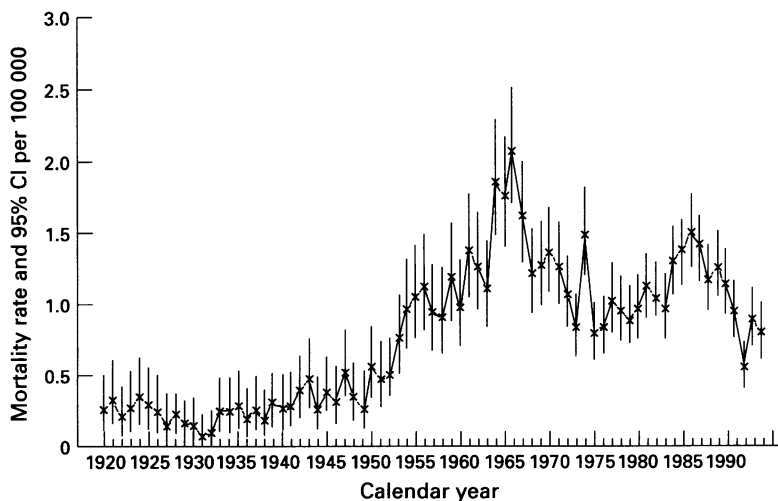


Figure 1 Asthma mortality in Australia, 1920–94, for both sexes aged 5–34 years.

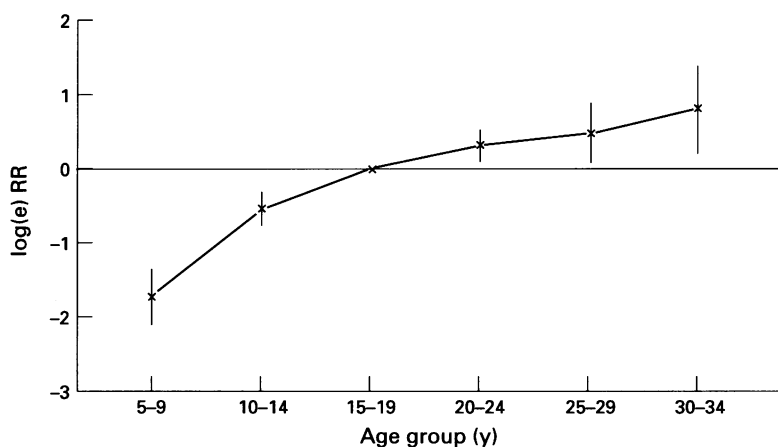


Figure 2 Asthma mortality in Australia, 1920–94, in both sexes aged 5–34 years. Effect of age adjusting for period and cohort effects.

and single calendar year 1920–94 were obtained from the Australian Bureau of Statistics.¹⁸ The *International Classification of Diseases* (ICD-9)¹⁹ code used for asthma was 490–496. Only ages 5–34 years were included in the analysis because of diagnostic difficulties outside of this age range using death certificate information,²⁰ and because this is the most common age range quoted in published reports.²¹ Both sexes were analysed together since there were no obvious differences in age adjusted period trends by sex, and to maximise numbers in the calculations. There are 3286 asthma deaths included in the analysis. Before 1940 there were ≤ 10 deaths annually, rising to a peak of 105 in 1966, with a subsequent decline, then again rising to ≥ 100 annually during the late 1980s.

For APC modelling, the data on asthma deaths and population were tabulated by five year age group and single calendar year, for the period 1920–94. Birth cohorts were identified which ran obliquely through the age-period data matrix. Age and cohort were in five year groups using mid decade and end decade divisions, but annual periods were employed because some of the period effects may be localised to particular years. Covering 75 years,

KEY POINTS

- Australia experienced two epidemics of asthma deaths between 1920 and 1994, one in the mid 1960s and the other in the late 1980s.
- Age-period-cohort modelling showed that some of the increase in asthma deaths in the mid 1960s and all of the late 1980s rise seemed to be a result of birth cohort effects.
- The increasing risk of asthma death with more recent birth cohorts is consistent with evidence of an increasing prevalence (and presumably incidence) of asthma in Australia.
- If increasing birth cohort trends continue, mortality will only be controlled by ever improving treatment, which may be difficult to sustain.

the data permitted six observations for each five year birth cohort in the body of the matrix. The most recent and the oldest three cohorts (extreme cohorts) were aggregated, producing 16 cohorts for analysis.

STATISTICAL ANALYSIS

The age specific asthma mortality data, 1920–94, for ages 5–34 years were age adjusted by the direct method²² using the 1991 census as the standard population. Confidence intervals were calculated using the Poisson distribution because of small numbers.²³

The APC modelling was achieved by Poisson regression:

$\log_e(c/p) = \beta_1 \text{ age} + \beta_2 \text{ period} + \beta_3 \text{ cohort} + k$
 where c = cases, p = population, k = constant, and the β s are the regression coefficients (\log_e relative risk) for the model.

To deal with the problem of non-identifiability, single year periods and five year age and cohort brackets were used. In addition, extreme cohorts were aggregated.

The data were modelled using *GLIM*.²⁴ Referent groups for age, period, and cohort were chosen to be around the middle of the categories. The coefficients (\log_e relative risk) for age, period, and cohort from the APC regressions were plotted, along with their 95% confidence intervals, to show the separate effects of age, period, and cohort in the model, controlling for the effect of the other two variables. The statistical contribution of each variable to the model was assessed by backwards deletion from the full model, and the resulting change in deviance was assessed as a χ^2 using the change in degrees of freedom to obtain the p value.

Results

Age standardised asthma mortality (fig 1) remained low ($< 0.5/100\ 000$) from 1920 to 1953, after which there was a sustained increase to levels around 1 per 100 000 from the mid 1950s to the mid 1960s. The mid 1960s epidemic of asthma deaths then ensued, which peaked at

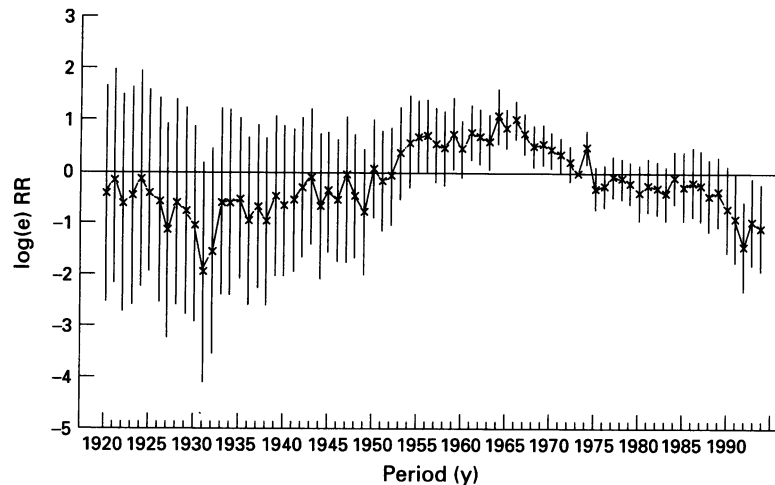


Figure 3 Asthma mortality in Australia, 1920-94, in both sexes aged 5-34 years. Effect of period adjusting for age and cohort effect.

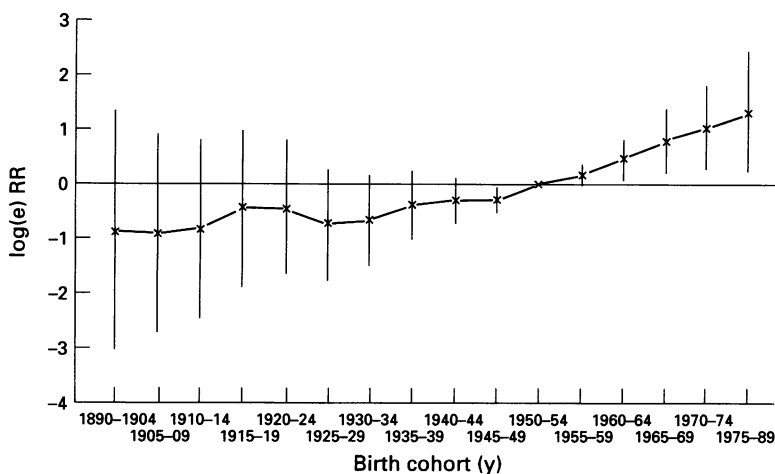


Figure 4 Asthma mortality in Australia, 1920-94, in both sexes aged 5-34 years. Effect of cohort adjusting for age and period effects.

around 2 deaths per 100 000. Death rates were back to 1 per 100 000 by the late 1960s, and, except for a single year peak in the mid 1970s, remained at that level until the late 1980s epidemic of asthma deaths which peaked at around 1.5 deaths per 100 000. By the early 1990s asthma death rates had returned to around 1 per 100 000.

The APC model was satisfactory, with a reduction in deviance from 2111 (df=449) for a nul fit, to 469 (df=355) residual for the full model. There were significant independent effects of all three variables, as determined by backward deletion from a full model. Age had the strongest effect ($\chi^2_{(5)}=212$, $p<0.001$), followed by period ($\chi^2_{(74)}=442$, $p<0.001$) and cohort ($\chi^2_{(15)}=57$, $p<0.001$).

The effects of age, period, and cohort (adjusting for the other two variables) are plotted in figures 2-4. The ages 5-9 and 10-14 years showed lower relative risks for mortality than ages 15-34 years (fig 2). A progressively increasing cohort effect was obvious from the birth cohort of 1950-54 onwards (fig 4). The plot of the period effect (adjusted for age and cohort) reveals an increase during the 1950s, a slight peak in the mid-1960s, a decline during

the 1970s (except for a single year peak), a flat trace during the 1980s, and a decline during the early 1990s (fig 3).

Discussion

Analysis of asthma mortality at a population level is complicated by the relatively small number of annual deaths, and consequently stochastic fluctuation, and by diagnostic difficulties when data are derived from death certificates. Misclassification bias can be limited by restricting analysis of asthma mortality to ages 5-34 years since this excludes confusion with other respiratory conditions of early childhood, and avoids the problem of differentiating asthma from the chronic airflow limitation disease complex in adults.²¹ Misclassification of year of death may also occur because of delays in notification or registration and coding. Such phenomena may account for the single year peak observed in 1974.

Changes in mortality rates over time may also occur as a result of misclassification bias through shifts in diagnostic labelling and coding criteria.²⁵ The change from ICD-5 to ICD-6 occurred in 1950, but the sustained rise in asthma mortality did not occur until 1953. Moreover, most of the 1950s increase was over before the introduction of ICD-7 in 1957.

Data for Australian asthma deaths for all ages indicates a sharp rise in 1950 with the change in ICD-5 to ICD-6 as cases of "Asthmatic Bronchitis" were recoded from bronchitis to asthma. However, there is no evidence to suggest this affected the 5-34 year mortality data. Thus, the rise in asthma deaths during the 1950s is unlikely to be a coding artefact, but could have been a consequence of changes in diagnostic labelling by medical doctors. The APC modelling implies that the 1950s increase is entirely a period effect which is consistent with this explanation. The increase in death rates could also have been treatment related, although this would be difficult to substantiate.

APC modelling presents difficulties because any one variable may be derived from the other two, producing the problem of non-identifiability. Although there is no ultimate solution to this problem, a unique solution in the regression analysis can be found by imposing certain restrictions. We used single period years and five year age and cohort brackets, and aggregated the youngest and oldest cohorts in order to permit Poisson regression analysis of the data. This may have had an impact on apparent patterns. Use of different width cohort and period brackets was also used by Burney¹⁷ to produce a unique solution to APC modelling of asthma mortality. Single period years are very useful in this type of analysis because period effects may be very brief (1-3 years), and may be disguised if they are divided by aggregations of calendar years (especially five year brackets). The use of five year brackets for age and cohort would disguise year to year variations in these variables.

The main finding of this analysis is that there seems to be an increasing birth cohort effect for asthma mortality for cohorts born in

1950–54 and later. This is consistent with an increasing putative aetiological influence which operates early in life, and renders successive cohorts more susceptible to asthma death. This finding is congruent with the increasing prevalence (and presumably increasing incidence) of asthma previously documented in the Australian population.⁴⁵ These findings are consistent with effects of increasing industrialisation and urbanisation, and focus attention on an environmental aetiology of asthma.²⁶ The aetiological influences in question may be due to the changes in home environments which foster the proliferation of human house dust mite¹¹ or gas heating or cooking,²⁷ or to changes in diet,²⁸ or host resistance.²⁸

The plot of the period effects (adjusting for age and cohort) suggests that the rise during the 1950s was a period effect, and could have been due to changing diagnostic labelling by medical doctors, although not due to coding changes (see above), or a treatment effect. When the cohort effect is subtracted, the mid 1960s peak of asthma deaths appears reduced, and the late 1980s increase in asthma deaths appears eliminated. The implication is that both periods of increased asthma deaths in an age-period analysis are mostly due to cohort effects, a suggestion previously put forward by Bauman and Lee.²⁹

It is interesting to note that immediately following the age adjusted period increases in asthma mortality (mid 1960s and late 1980s), a decline occurred in the period effect (adjusted for age and cohort). This could be interpreted as a consequence of an improvement in clinical asthma management, particularly use of preventive therapy such as inhaled steroids for the most recent epidemic which appears to have been spurred on by the preceding (cohort) increases in deaths.

Aerosol bronchodilators have been widely available in Australia since the 1960s—without prescription in NSW since 1976 and in all states since 1985.³⁰ There have been suggestions that clinical management practices favouring their use, and/or particular ingredients (isoprenaline in the 1960s, fenoterol in the 1980s) may have been associated with the two (period) peaks in asthma mortality. The evidence for this is stronger for the mid 1960s epidemic in deaths, which seems to be both a period and cohort phenomenon, than the late 1980s epidemic, which appears to be almost entirely a cohort effect. Furthermore, although fenoterol was implicated in the rise and fall of asthma mortality in New Zealand during the 1980s,⁹ use of this drug in Australia was very low indeed. Although use of bronchodilator aerosols increased in Australia during the 1980s,³⁰ probably due to both an increased prevalence of asthma and increased drug treatment of it, the pattern of increased consumption preceded the late 1980s epidemic in deaths. However, the late 1980s decline appears to be a period effect, supporting the efficacy of asthma management plans based

on preventive medication rather than bronchodilators.

The implication of these findings is that in the future it will be necessary to continue to improve asthma management in order to even maintain flat mortality for future periods in the face of an ever increasing cohort effect. Moreover, research and development into environmental causes of asthma and their control is urgently needed.

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